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Revive Comprehensive Program, But Don't Tie It To Grant Review, Center Executives Agree

Directors and other executives of cancer centers generally agreed that the dormant NCI comprehensive cancer centers program should be revived and made meaningful, but there was

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In Brief

Hammer Reappointed Chairman; Wyngaarden Names Ferguson of Baylor As OMAR Director

ARMAND HAMMER, two months after his 90th birthday, was appointed by President Reagan to another one year term as chairman of the President's Cancer Panel. An M.D. (Columbia, '21) who has never practiced medicine, the chairman and CEO of Occidental Petroleum has contributed millions to cancer and other biomedical research and currently is heading a drive to raise $500 million for NCI from the private sector with the understanding that Congress will match that amount. The Panel, which also includes William Longmire and John Montgomery, will hold its next meeting Sept. 19 at the Arizona Cancer Center in Tucson. . . . **JOHN FERGUSON**, associate clinical professor of neurology and family practice at Baylor College of Medicine in Waco, has been appointed director of the NIH Office of Medical Applications of Research by NIH Director James Wyngaarden. The job includes heading up the NIH Consensus Development Program, coordination of Medicare coverage issues and the NIH patent program. . . . **GROUND BREAKING** ceremony for the Children's Inn at NIH was scheduled for July 29. To be built on a two acre wooded site on the NIH campus, the Inn will house up to 36 families of pediatric patients being treated in research programs at NIH. Merck & Co. contributed $2.3 million for the construction . . . . **HOSPITAL CANCER** programs approved by the American College of Surgeons Commission on Cancer now total 1,211, following the most recent round of approvals. . . . **GEORGE CANELLOS**, chief of medical oncology at Dana-Farber Cancer Institute, has been named the first William A. Rosenberg Professor of Medicine at Harvard Medical School and the Institute. Rosenberg, founder of Dunkin' Donuts, endowed the professorship; he is a cancer survivor, who became a patient of Canellos in 1977 when he was diagnosed with lymphoma. . . **THOMAS HAYNIE**, chairman of the Dept. of Nuclear Medicine at UT M.D. Anderson Cancer Center, has been appointed to the James E. Anderson Professorship in Nuclear Medicine there.

Centers Want Active Comprehensive Program; Key Element Is More Money

(Continued from page 1)
little enthusiasm for the staff generated proposal to make recognition (or designation) of comprehensive status dependent on successfully competing for a comprehensive center core grant.

Leaders from most of the 60 NCI supported cancer centers met in Washington last week with the National Cancer Advisory Board's Centers Committee to discuss the proposals submitted to the committee in April (**The Cancer Letter**, April 29).

The key element of those proposals was the suggestion that recognition as comprehensive be achieved through the award of a comprehensive center support, or core, grant, using the NIH mechanism known as the P60 grant.

NCI has not used the P60, going instead with the P30 for center core grants. Comprehensive designation was achieved following a request from the center and review by the NCAB and NCI staff members. If the NCAB recommended approval, it was then up to the NCI director to make the final determination. This process has not been used since 1979, when Columbia Univ. became the last center to be recognized as comprehensive.

The new proposal also included updated characteristics for centers to possess in order to be considered comprehensive. Last week's meeting also considered them.

John Durant, chairman of the Centers Committee, summarized "what I thought I heard" during the day and a half meeting:

"First, what I thought I heard, was that the P60 is not a bad idea but you don't like the idea of tying it to comprehensive status.

"Second, that comprehensiveness should be taken seriously by NCI and the NCAB, and review should be done periodically.

"Third, the new tasks (proposed by staff), the requirements for participation in high priority clinical trials, cancer control, and training, should be accepted.

"Fourth, the criteria that have been put forth, give or take some, are about right, although they may need some clarification or modification.

"Fifth, there is a real desire for partnership and collaboration with NCI, along the lines recommended by the AACI (Assn. of American Cancer Institutes in a statement drafted by Richard Steckel, director of the UCLA Jonsson Comprehensive Cancer Center).

"Sixth, if cancer control is to be done, there is a real need for an academic target for this money." The problem could be addressed, Durant suggested, with "judicious use of P20s (planning grants) to develop the required academic structures."

The overriding problem, Durant concluded, "is money. The veteran (Washington observers) understand that you get the money from Congress with new packages. You excite donors with something new, something you believe can be accomplished."

Durant was suggesting that a revamped comprehensive cancer centers program, with updated tasks (or criteria, or characteristics) and with recognition as comprehensive automatic with the award of a new type of core grant, could generate enthusiasm in Congress and a willingness to support the program with new money.

Some center representatives expressed opposition to a requirement for taking part in national, high priority clinical trials. Who determines what is high priority bothered them, and some also felt that centers are more useful in developing creative new pilot studies rather than the large scale phase 3 trials.

Sydney Salmon, whose letter requesting consideration for comprehensive status triggered the update discussions, challenged the contention that centers should not be required to participate in high priority clinical trials.

"If a clinical center is unwilling to participate in one or more high priority trials because it thinks that is not its mission, it ought to rethink its mission. That goes in spades for a comprehensive center," Salmon said.

Steckel suggested that the review for comprehensiveness should be carried out separately from the core grant review, insisting that it should be rigorous and repeated at certain intervals "if the term comprehensive is to mean anything."

Ronald Herberman, as director of "the latest center to be recognized by NCI (Pittsburgh Cancer Institute) and one that hopes to develop into a comprehensive cancer center," said he did not agree with Steckel on separating the two reviews. "We spend too much time being reviewed. If appropriate guidelines are given to the site visitors," they could carry out both reviews at once, he said.

A full report on discussion of the issues at the meeting will appear in next week's issue of ***The Cancer Letter.***

OSU, Hawaii Name New Center Chiefs; Berlin Acting Director At Miami

Major developments in cancer center leadership have recently occurred:

*David Schuller, who has been director of the Head and Neck Conology Program of the Ohio State Univ. Comprehensive Cancer Center, has been appointed to the twin positions of director of the center and director of the new Arthur B. James Cancer Hospital & Research Institute at OSU.

David Yohn, director of the center since it was established 15 years ago, remains as deputy director. Stanley Balcerzak, the deputy since 1984, is now associate deputy director. Remaining as associate directors are Gus Cavalaris, cancer prevention; Michael Grever, interdisciplinary clinical oncology; and Donald Witiak, basic research.

*Brian Issell, formerly vice president for research at Cetus Corp. and clinical professor of medicine at Stanford Univ. and the Univ. of California (San Francisco), has been appointed director of the Cancer Research Center of Hawaii. The center is part of the Univ. of Hawaii (Manoa). Issell will also hold appointments as professor of medicine and chief of oncology at the John A. Burns School of Medicine. He will begin his new position Sept. 1

*Nathaniel Berlin, who has been deputy director of the Papanicolaou Comprehensive Cancer Center at the Univ. of Miami, is now the acting director, with the retirement of Gordon Zubrod. A search committee has been formed to find a permanent director. Berlin formerly was director of the Northwestern Univ. Cancer Center.

*John Kmet, senior VP at Miami (Ohio) Valley Hospital, is the new administrator of Hipple Cancer Research Center in Dayton.

Breast Cancer Overview Correlates Incidence Increase With Other Factors

NCI's Div. of Cancer Prevention & Control compiled a comprehensive overview of breast cancer research, largely in response to an apparent increase of 21 percent in age adjusted incidence rates from 1980 to 1985.

The overview looked at possible correlations between the increase and changes in known risk factors, diagnosis and screening. That portion of the overview covering the background of the situation and epidemiology was published in last week's issue of The Cancer Letter. The overview of breast cancer research in prevention, carcinogenesis and biology follows:

Prevention

There is increasing emphasis on breast cancer prevention through studies on diet, nutrition and chemoprevention.

The relationship of dietary, nutritional and life style factors to breast cancer with the goal of developing ways to prevent this disease is under study. One study addresses aspects of the western diet associated with breast cancer risk in American women of Asian ancestry, and will evaluate whether dietary factors during childhood and adolescence are crucial risk factors. A joint U.S.-Finland study of nutrition and cancer is examining the role of fats, selenium and vitamins A, E and C in breast cancer development or suppression. Research is continuing in an effort to identify blood markers that reflect dietary intake. Such markers would aid future studies of dietary fat modification in breast cancer prevention.

Chemoprevention is receiving increasing attention. Studies are supported emphasizing inhibition, arrest, reversal, or delay of mammary carcinogenesis in established rat and mouse models. The use of selected micronutrients such as vitamins is a major area of study. Several compounds are being evaluated to determine if they can inhibit the development of cancer. Substances that have exhibited protective effects in animals include retinoids, vitamin E and selenium. The interaction of preventive agents and hormones is also under investigation.

A program is under way to test the effects of chemopreventive agents on experimental mammary cancer induced in animals with DMBA or NMU. Agents being tested include 4-HPR (a synthetic retinoid) and four other retinoids, selenium (Na selenite, Na selenate, selenomethionine), molybdenum, vitamin E, ellagic acid, DFMO, oltipraz and fluocinolone, and various combinations of some of these. Other agents or substances under investigation include inorganic and organic forms of selenium, carotene, nationally occurring steroidal compounds and steroid derivatives, orange oil and components of orange oil, inhibitors of fatty acid metabolism and compounds of vanadium.

The investigations emphasize basic mechanisms of action of chemopreventive compounds coupled to demonstration of anticarcinogenic efficacy. Some studies

modulate the dietary and nutritional status of the host, most notably in fat and energy intake, as part of the inquiries.

A clinical study is under way to test the effectiveness of 4-HPR in reducing breast cancer recurrence in women who have had their primary tumors removed and now appear to be clinically free of disease.

Other studies are concerned with modification of eating behavior in the community with the aim of developing interventions toward modifications in the direction of NCI's dietary guidelines. The NCI/Giant Food supermarket intervention study is aimed at modifying consumer purchasing behavior through specific labeling regarding content of fat, fiber and certain other specific diet components. Three states funded under the initiative, "Technical Development in Public Health Agencies," have in progress programs on dietary modification for cancer prevention, addressing NCI's Year 2000 goals.

Carcinogenesis

Carcinogenesis studies of mammary cancer continue to receive emphasis. Several projects are examining the role of polyunsaturated dietary fatty acids in mammary gland tumorigenesis in animal models. The influence of quantity and type of fatty acids on the development of tumors in the mammary gland is being investigated. Also under study is the role of hormones in the induction of mammary tumorigenesis by dietary fat.

Other projects within the area of diet and nutrition explore additional life style factors which may play a role in mammary gland tumorigenesis. One project is seeking to determine whether or not chronic caffeine consumption by laboratory animals contributes to the development and progression of mammary gland neoplasia. In another study, a mammary tumor model is being developed which would address epidemiological data reporting risk associated with alcohol. Possible mechanisms of carcinogenesis by alcohol are also being explored.

Other studies are examining dietary components that promote experimental mammary tumorigenesis and possible mechanisms by which they may accomplish this, as well as mechanisms for reducing this effect. Under study are high and low fat diets, high and low dietary protein, type of fat and mechanisms of enhancement of mammary tumor development by omega-6 polyunsaturated fatty acid, inhibition of tumorigenesis by omega-3 unsaturated fatty acids, as well as prevention of mammary tumorigenesis by dietary molybdenum. Nipple aspirate breast fluid from mice is being used to follow exposure of breast epithelium to carcinogens or protective agents.

The carcinogenesis mechanisms area is exploring the mechanism of mammary gland tumorigenesis induced by N-substituted aryl compounds in a rat model system. The role of one electron oxidation in the activation of these compounds is being elucidated.

Other projects are developing tissue culture models for the study of breast carcinogenesis. The objectives are to study the nutritional requirements of normal human and rat epithelial cells, and to determine the hormone and growth factor requirements of preneoplastic and neoplastic cells. Molecular genetic approaches to hormonal carcinogenesis are being pursued to elucidate how hormones control growth and expression of differentiation in normal and hormone dependent breast cancer.

Studies are also being pursued on the molecular and genetic mechanisms of mammary cell transformation by chemicals. The frequency of initiation and the role of oncogenes, retroviral and normal cellular genes in the initiation of malignancy are being investigated. Whether oncogene activation is an early event in cell transformation is also being probed.

Additional studies address the mechanisms of activation of carcinogens by mammary epithelial cells. The characterization of metabolites of polycyclic aromatic hydrocarbon carcinogens and the resultant carcinogen-DNA adducts should provide insight into the mechanism of activation of these chemicals to mutagenic and carcinogenic compounds.

Mouse mammary tumor viruses induce tumorigenesis in females at a very high rate. They exist both as milk transmitted exogenous viruses and genetically transmitted endogenous viruses. Studies concerned with endogenous virus attempt to understand the mechanism of tumor production. Two mouse strains of differing susceptibility are observed for differences in the oncogenicity of the virus and differences in the regulation and expression of what seem to be the same proviruses. The host's cellular genes that become activated by the insertion of the virus are being cloned and the temporal appearance of the protein products of those genes are being studied to identify the steps involved in transforming a normal breast epithelial cell into a neoplastic one. One of the major genes under investiga-

tion is the oncogene int-1 which appears to be implicated in the tumorigenic process and may be specific for mammary cells. The mechanisms of oncogenesis by this int-1 and its product are being studied by transduction of the oncogene into mammary epithelial cells in vitro by retroviral vectors.

Various oncogenes, such as erbB, H-ras, myc and SV40 large T-antigen gene are being transfected into normal and preneoplastic mammary cells to determine how disruption of growth signal transductions lead to unrestrained cell growth. The regulation of MMTV expression in normal mammary epithelium of virgin mice and in nonpregnant, nonlactating parous mice are studied to understand how the control of MMTV expression translates into the observed increased incidence of mammary tumorigenesis in parous mice. Others are studying a hormonally dependent benign breast fibroadenoma induced by injection of newborn Wistar/Furth rats with adenovirus 9, with interest in determining if the virus induced the tumors directly or by interaction with other host factors.

Specific aspects of glucocorticoid regulated transcription of proviral genes of MMTV are being investigated to elucidate the genetic and molecular bases of enhanced mouse susceptibility to mammary carcinomas under steroid hormonal influence.

Other investigations are being conducted with the mammary tumor virus to determine sequences in the human genome with homology to MMTV, frequency and distribution of such virus to identify sequences in normal and malignant human breast cells, which germ line MMTV provirus(es) affect spontaneous experimental mammary cancer, and to study how viral genes and hormones interact to produce transformation of preneoplastic lesions to mammary cancer in experimental model systems.

Other environmental carcinogenesis studies include radiation effects. Studies of radiation in relation to breast cancer include a long term followup of a cohort of women treated for post partum mastitis by x-rays, compared with women treated by other means, as well as basic studies of cellular and molecular changes in breast cells as a result of radiation exposure. Quantitative mammary cell transplantation techniques are being applied to investigate the effects of physical factors, such as radiation type, and biological factors, such as the role of hormonally controlled proliferation and differentiation, on cell survival, post irradiation repair and neoplasia.

By studying radiation and chemical induced leukemia in RF/Un mice and mammary tumors in BALB/cfC3H mice, the origins and role of oncogenes identified following radiation exposure are being elucidated, including determination if radiation induced ongogenes are similar to those associated with viral or chemical exposures. Sequential changes in mammary tissue following irradiation that lead to tumor formation are being observed and compared with changes following exposure to chemical carcinogens. Interaction between chemical and radiation exposures are also being studied in relation to carcinogenesis.

Cancer Biology

A broad spectrum of research programs examine the biology and immunology of breast cancer addressing basic mechanisms that may explain the differences between normal and neoplastic breast cells. These studies include the disciplines of cell biology, biochemistry, molecular genetics, endocrinology and pathology. They utilize both in vitro and animal models.

The search for oncogenes has generated important information to help explain certain abnormal characteristics in cancer cells. One such oncogene, HER-2/neu, was first detected in a mammary carcinoma cell line and now has been found at greatly increased levels in primary human breast cancer. This oncogene is related to another described several years ago (the erb-B gene) which codes for the receptor for epidermal growth factor. The consistent finding that oncogenes are related to growth factors is strong evidence for the contention that tumor cells growth in an uncontrolled manner because they have developed their own autocrine stimulation systems.

In order to more specifically identify the gene or combination of genes required to make a breast cell neoplastic, systematic studies are under way to transfect (or insert into) normal cells with various oncogenes such as ras and erb-B, previously demonstrated to be associated with human cancers to induce these genes to express their protein products, and to systematically monitor their influence in transforming the cells. Another class of genes that are equally important are the newly described suppressor genes that seem to be required to maintain the phenotype of normal cells. These are genes that are missing in neoplastic cells. One such suppressor gene, NM23, may be a natural cellular suppressor gene for the metastatic phenotype. The levels

of NM23 have been shown to correlate inversely with the metastatic aggressiveness of human breast carcinomas; high NM23 levels are associated with a good prognosis.

Sophisticated new techniques in molecular genetics have made experiments possible that once seemed impossible. A recent development in genetic manipulation is the ability to produce live mice carrying foreign genes in all their tissues and cells by inoculating the mouse egg with the experimental gene and then replacing the egg in utero so it matures normally. Such "transgenic" mice carrying sections of the virus MMTV do not develop tumors throughout their bodies but the tumors appear confined to mammary tissue. The information within the gene for such tissue specificity could be very important in helping to understand why cancer develops in different organs in different patients. Further, these special mice are providing a new understanding of the complex interactions of tumor induction at the molecular level. They can also be bred to produce offspring that continue to carry the foreign genes for additional experiments.

Other investigations are targeted at understanding the interactions between the neoplastic mammary epithelial cell and other normal cells and connective tissues in the same local environment in the breast. Immune effector cells that should be active in controlling abnormal epithelial growth, such as natural killer cells or special macrophages, seem to be reduced in number or to be unable to elicit the killing activity in several mouse model systems. This suppression of the immune system is under active study. Aggressive breast cancers which are metastatic produce their own enzymes and factors that allow them to dissolve away the extracellular matrix in which they are bound. They regulate their own movement away from the primary tumor by expressing a special factor, autocrine motility factor, the mechanism of which has already been partly determined; they over produce special proteins on their cell surface, called laminin receptors, that allow them to attach to the wall of a blood vessel and gain access to the circulating blood, the first step in metastasis. Each of these steps involves specific molecules which are the subject of intense investigation. Of great clinical potential is the possibility of finding inhibitors for these molecules that could be used in therapy. An inhibitor of the AMF already has been discovered and may enter clinical trials this year.

Another critical area of basic research on breast cancer seeks information about the hormonal regulation of normal breast cell growth and differentiation into milk producing cells and the loss of this regulation in human malignant cells. Emphasis is being placed on attempts to better understand the mechanism whereby the steroid hormones, estrogen and progesterone and even androgens and glucocorticoids regulate mammary growth. Cellular protein receptors for each steroid have been cloned and specific amino acid sequences of the cell's genomic receptor regions that actually bind unique sequences of the cell's genomic DNA have been identified for some receptors. It is clear that the effect of one steroid can be to activate the effects of another steroid and that estrogen is able to regulate the synthesis and secretion of a number of other protein growth factors, including insulin like growth factors 1 and 2 and tumor growth factors alpha and beta. The increased expression of EGF receptor in tumor cells appears also to be modulated by the sex steroids. Some of these growth factors exert stimulatory effects on mammary cell growth and others, especially TGF beta, have been shown to suppress normal epithelial cell growth in the mammary gland of the live mouse.

Additional studies are focusing on the influence of local factors produced by tumor cells on adjacent adipose cells in the mammary gland. These factors seem able to elicit the fat cells' assistance by promoting the enzymatic interconversion of androgens and estrogens utilized by the tumor cells for their rapid growth. In similar experiments, mammary stromal fibroblasts in direct cell contact with tumor cells promote estrogen effects in the mammary cells, including cell proliferation. Whether this cell to cell interaction results from exchange of diffusible molecules or is related to other signals is under investigation.

Breast cancer cells also synthesize factors that promote resorption of bone and induce hypercalcemia which contributes further to the complications of breast disease. These factors seem related to an increased dependence on calcium for growth of these cells. Some evidence now suggests that calcium antagonists are able to inhibit growth of these cells both in vitro and in vivo.

The DCPC overview of breast cancer research in detection and diagnosis, and treatment, completing the report, will be published next week in ***The Cancer Letter.***

NCI Advisory Group, Other Cancer Meetings For August, Sept., Future

Cancer Therapeutics Program Project Review Committee--Aug. 9-10, Holiday Inn, Chevy Chase, MD, open Aug. 9, 8-8:30 a.m.

Cancer Centers Support Review Committee--Aug. 11-12, Crowne Plaza Holiday Inn, Rockville, MD, open Aug. 11, 8:30-9:30 a.m.

Physician Update on Cancer, AIDS, and Liver Disease --Aug. 12-14, Timberline Four Seasons Resort, Davis, WV. Contact Kathryn Saumure, c/o Frederick Reichle MD, Presbyterian Univ of Pennsylvania Medical Center, 39th and Market Streets, Philadelphia 19104, phone 215/387-3685.

Fine Needle Aspiration--Aug. 13-20, Maui. 8th annual symposium. Contact Univ. of California School of Medicine, Rm 569-U, San Francisco 94143, phone 415/476-4251.

International Society for Experimental Hematology--Aug. 21-25, Westin Galleria Hotel, Houston. 17th annual meeting. Contact Carol Knight, Conference Services, Box 131, Univ. of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston 77030, phone 713/792-2222.

Supportive Care in Oncology--Aug 23-25, Palais des Congres, Brussels. First international conference. Contact ICSCO Desk, SYMEDCO, 900 State Rd., Princeton, NJ 08540, phone 1-800/821-5678 (609/683-1505 from New Jersey and outside the U.S.).

Cancer Management Course--Aug. 26-27, Charleston, WV. Contact Dr. Eric Mantz, Cancer Dept., American College of Surgeons, 55 E. Erie St., Chicago 60611, phone 312/664-4050.

Cancer Care: Increasing the Odds--Aug. 26-27, Harrah's Marina Casino, Atlantic City. Contact Richard Attilio, RPh, MS, Comprehensive Community Cancer Center, 17th and Chew Streets, Allentown, PA 18102, phone 215/776-8880.

Fifth World Conference on Lung Cancer--Aug. 28-Sept. 1, Interlaken, Switzerland. Contact Dr. R.A. Joss, Institute for Medical Oncology, Inselspital, 3010 Berne, Switzerland.

European Tissue Culture Society--Aug. 31-Sept. 2, Gent, Belgium. 36th meeting. Contact ETCS Gent 1988, c/o Prof. L. de Ridder, Louis Pasteurlaan 2, 9000 Gent, Belgium.

Fifth International Conference on Cancer Nursing--Sept. 4-9, London. Contact Christine James, Macmillan Journal Ltd., 4, Little Essex St., London WC2R 3LF, UK.

International Academy of Pathology--Sept. 4-9, Dublin. XVII International Congress. Contact IAP, 44 Northumberland Rd., Dublin 4, Ireland.

European Society for Therapeutic Radiology and Oncology--Sept. 5-8, Den Haag, The Netherlands. Seventh annual meeting. Contact ESTRO Secretariat, Dept. of Radiotherapy, University Hospital St. Raphael, 3000 Leuven, Belgium.

Breast Issues 1988: Challenges and Choices--Sept. 6-9, Sheraton Denver Tech Center, Denver. Contact Joan Camp, Conference Planner, Nancy Gosselin Foundation for Breast and Other Women's Health Issues, 800 E. Belleview, Mailbox #3, Central Tower, Englewood, CO 80111, phone 303/972-1706.

Fundamental Tumor Registry Operations--Sept. 7-9, Springhill Memorial Hospital, Mobile, AL. Contact local coordinators Karen Wilson, 205/460-5274, or Diane Bass, 205/460-5251.

Molecular Diagnostics of Human Cancer--Sept. 7-11, Cold Spring Harbor, NY. Contact Registrar, Cold Spring Harbor Laboratory, Bungtown Rd., Cold Spring Harbor, NY 11724, phone 516/367-8343.

Radioimmunodetection and Radioimmunotherapy of Cancer--Sept. 8-10, Princeton, NJ. Second conference. Contact Robyn Kohn, Center for Molecular Medicine & Immunology, 1 Bruce St., Newark, NJ 07103, phone 201/456-4600.

Cancer Management Course--Sept. 9-10, Houston. Contact Dr. Charles Balch, Cancer Dept., American College of Surgeons, 55 E. Erie St., Chicago 60611, phone 312/664-4050.

Research on Human Tumor Antigens--Sept. 12, Dayton, OH. Contact Nancy Zimmerman, Dayton Oncology Society, 4100 S. Kettering Blvd., Dayton 45439, phone 513/293-8508.

Diagnostic Cytopathology Course--Sept. 12-14, New York. Contact Steven Hajdu, MD, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021, phone 212/794-7999.

Intraoperative Radiation Therapy--Sept. 12-13, Innsbruck, Austria. Second international symposium. Contact Prof. Dr. E. Bodner, 2nd Surgical Dept., Prof. Dr. H. Frommhold, Dept. of Radiation Therapy, Univ. of Innsbruck, Anichstr. 35, 6020 Innsbruck, Austria.

Cancer Nursing Strategies: Today and Tomorrow--Sept. 13-16, Westin Galleria Hotel, Houston. Contact Conference Services-HMB 131, UT M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston 77030, phone 713/792-2222.

Modern Approaches to New Vaccines Including Prevention of AIDS--Sept. 14-18, Cold Spring Harbor. Contact Registrar, CSH Laboratory, Bungtown Rd., Cold Spring Harbor, NY 11724, phone 516/367-8343.

Soft Tissue Tumor--Sept. 15-17, New York. 8th annual symposium. Contact Steven Hajdu, MD, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021, phone 212/794-7999.

Breast Cancer 1988: Clinical and Basic Science Advances--Sept. 15-17, Dallas. Contact Barbara Grayson, Office of the Dean, Baylor Univ. Medical Center, 3500 Gaston Ave., Dallas 75246, phone 214/820-2317.

VIII Brachytherapy Update--Sept. 16-17, New York. Contact Roberto Fuenmayor, CME Planning Office, C-180, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021, phone 212/794-6754.

American Society of Pediatric Hematology/Oncology --Sept. 16-18, Chicago. First annual meeting. Contact Dr. Carl Pochedly, Wyler Children's Hospital, 5841 S. Maryland Ave., Chicago 60637, phone 312/702-6808.

President's Cancer Panel--Sept. 19, Arizona Cancer Center, Tucson, 9 a.m., open.

Regulation of Growth and Differentiation in Pancreative Cancer--Sept. 19-20, Marriott Hotel, Bethesda. Organ Systems Program workshop. Contact Dr. Harold Asch, Organ Systems Coordinating Center, Roswell Park Memorial Institute, 666 Elm St., Buffalo, NY 14263, phone 716/845-2317.

Problems of Diagnosis and Therapy of Endometrial Cancer--Sept. 20-23, Eisenach, German Democratic Republic. Contact Medical Academy of Erfurt, Dept. of Gynecology and Obstetrics, Gorkistr. 6, 5020 Erfurt, GDR.

Transrectal Ultrasound in the Diagnosis and Management of Prostate Cancer--Sept. 23-24, Chicago. Third international symposium. Contact Diversified Conference Management Inc., PO Box 2508, Ann Arbor, MI 48106, phone 313/665-2535.

Advances in Chemotherapy of AIDS--Sept. 23, Univ. of Alabama (Birmingham). Organized by the Div. of Clinical Pharmacology. Contact CME Office, phone 205/934-2687 or 1-800/231-0507.

National Cancer Advisory Board--Sept. 26-28, Bethesda. NIH Bldg 31 Rm 6. Open Sept. 26 and 28, closed Sept. 27 for review of grants. Committee meetings to be announced.

Cancer Biology and Immunology Contract Review Committee--Sept. 26, Guest Quarters Hotel, Bethesda, open 9-9:30 a.m.

Challenges of Oncology Nursing--Sept. 28-30, Bunts Auditorium, Cleveland Clinic Foundation. Contact Dept. of Continuing Education (TT31), Cleveland Clinic

Educational Foundation, 9500 Euclid Ave., Cleveland, OH 44195, phone 444-5695 (local); 800/762-8172 (Ohio); 800/762-8173 (elsewhere).

Fundamental Tumor Registry Operations--Sept. 28-30, Chesterfield, MO. Contact Local Coordinator, Bonnie Lehmann, 314/434-1500 Ext. 4018.

American College of Epidemiology--Sept. 28-30, Ann Arbor, MI. Annual scientific symposium. Contact Dr. Curtis Mettlin, Roswell Park Memorial Institute, 666 Elm St., Buffalo, NY 14263.

European Groups on Head and Neck Cancer Studies--Sept. 28, Paris. 12th plenary session. Contact Dr. J.L. Lefebvre, Head & Neck Oncology Dept. Centre Oscar Lambret, Rue F. Combemale, BP 307, 59020 Lille, France.

New Directions: Responding to the Needs of Oncology Social Workers--Sept. 29-30, Holiday Inn Crowne Plaza, Orlando, FL. Contact Kimberly Kauss, BSW, 1988 Conference Chairperson, Dept. of Social Work, Florida Hospital Altamonte, 601 E. Altamonte Ave., Altamonte Springs, FL 32701, phone 407/830-4321 Ext. 2209.

Cancer Programs: Maintaining the Momentum for Success--Sept. 29-30, Mariner's Inn, Hilton Head Island, SC. Contact Ron Gilden, CDP Inc., 5901 Peachtree Dunwoody Rd., Suite C100, Atlanta, GA 30328, phone 404/391-9872.

Chemically Contaminated Aquatic Food Resources and Human Cancer Risk--Sept. 29-30, Conference Center, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Contact Martha Taylor, Office of the Senior Scientific Advisor to the Director, NIEHS, RTP, NC 27709.

FUTURE MEETINGS

Cancer Program Planning Workshop--Oct. 6-7, Mariner's Inn, Hilton Head Island, SC. Sponsored by Cancer CarePoint Inc. for hospital administrators and cancer care professionals who are developing cancer centers or wish to enhance cancer programs. Contact Nancy Reid, Cancer CarePoint, 2394 Mt. Vernon Rd., Suite 200, Atlanta, GA 30338, phone 404/399-1812.

Control of Cell Proliferation and Cancer--Oct. 13-14, Royal Sonesta Hotel, Cambridge, MA. 1988 symposium. Contact Office of Continuing Education, Tufts Univ. School of Medicine, 136 Harrison Ave., Box 36, Boston, MA 02111, phone 617/956-6579.

DNA Probes: Market Challenges and Opportunities--Oct. 25, Marriott Hotel, San Diego. Executive conference. Contact Communitech Market Intelligence, PO Box 67, Yorktown Heights, NY 10598, phone 914/245-7764.

Scripps Memorial Hospitals 12th Annual Cancer Symposium--Nov. 7-9, Sheraton Harbor Island Hotel, San Diego. Also concurrently, Cancer Symposium for Nurses. Contact Nomi Feldman, Cancer Symposium Coordinator, 3770 Tansy, San Diego, CA 92121, phone 619/453-6222.

Directions in Pediatric Hematology/Oncology Care--Nov. 17-19, Harbour Island Hotel, Tampa. Contact Cindi Butson, Seminar Coordinator, FAPTP, PO Box 13372, University · Station, Gainesville, FL 32604, phone 904/375-6848.

Chromosomes in Solid Tumors--Feb. 26-28, 1989, Doubletree Inn, Tucson. Third international symposium. Abstract deadline is Dec. 1. Contact Mary Humphrey, Conference Coordinator, Arizona Cancer Center, Tucscon, AZ 85724, phone 602/626-2276.

Advances in Clinical Oncology--March 11-17, 1989, Snowbird, UT. Seventh winter symposium. Contact Mary Humphrey, Conference Coordinator, address and phone above.

RFAs Available

RFA 88-CA-15

Title: Prevention clinical trials utilizing intermediate endpoints and their modulation by chemopreventive agents

Application receipt date: Oct. 13

The Div. of Cancer Prevention & Control invites applications for cooperative agreements to support clinical trials which are directed toward examining the role of various chemopreventive agents and/or diet in the prevention of cancer. This is a followup to earlier RFAs which had requested grant and cooperative agreement applications.

The major objective of this RFA is to encourage cancer chemoprevention clinical trials which utilize biochemical and/or biological markers to identify populations at risk and/or to provide intermediate endpoints that may predict later reduction in cancer incidence rates.

These studies may be developed in phases, including a pilot phase, which could later proceed to a full scale intervention. The main emphasis should be on small, efficient studies aimed at improving future research designs of chemoprevention trials, providing biologic understanding of what is happening in the trials, or providing better, more quantitative and more efficient endpoints for these trials. After successful completion of the pilot phase (ie.e. demonstrated modulation of marker endpoints by the intervention), subsequent studies can include phase 3 clinical trials involving the designated agent, the utilization of the monitoring test system and a cancer incidence or mortality endpoint.

Investigators may apply at this time for the pilot phase, or submit an application for both phases. However, if the application is for the pilot phase only, the proposed study must describe its relevance to a clinical application and utilize a chemopreventive agent, marker test system, and study population which could later be the subject of a full scale, double blind, randomized, risk reduction clinical trial.

Applicants funded under this RFA will be supported through the cooperative agreement mechanism. An assistance relationship will exist between NCI and the awardees to accomplish the purpose of this activity. The recipients will have primary responsibility for the development and performance of the activity. However, there will be government involvement with regard to (1) assistance in securing investigational new drug approval from the Food & Drug Administration; (2) monitoring of safety and toxicity; (3) coordination and assistance in obtaining the chemopreventive agent; (4) quality assurance with regard to the clinical chemistry aspects of the study.

Awards will not be made until all arrangements for obtaining the IND, agent, and its delivery are completed. Final awards will also consider not only the cost of the clinical trial but also the cost of the agent and its formulation if necessary.

Approximately $1 million in total costs per year for three years will be committed to specifically fund applications which are submitted in response to this RFA. It is anticipated that three to five awards will be made annually. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit.

Complete copies of the RFA and further information may be obtained from Marjorie Perloff, MD, Chemoprevention Branch, Blair Bldg. Rm. 616, NCI, Bethesda, MD 20892, phone 301/427-8680.

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